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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/561,033

12/16/2005

Leifeng Cheng

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ROPES & GRAY LLP

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EXAMINER

TUCKER, ZACHARY C

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/561,033	Applicant(s) CHENG ET AL.	
	Examiner Zachary C. Tucker	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10, 12 and 15-17 is/are pending in the application.
4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 12 and 15-17 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>16Dec05</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first and second paragraphs of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of obesity, bulimia and extended abuse, addiction, and/or relapse indications, does not reasonably provide enablement for the treatment of all of the other indications recited in those claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

When considering whether a claimed invention is enabled by the supporting disclosure, the Office customarily relies on the factors put forth in the decision rendered for *In re Wands*, which are:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731,737 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

Each will be addressed, with respect to the rejection at hand.

- (A) Claims 15 and 16 are quite broad; they read on treatment of a variety of specific

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conditions, and also, treatment of “psychiatric disorders,” “cognitive disorders,” “memory disorders,” “attention disorders,” “and related disorders,” “neurological disorders,” “immune cardiovascular, reproductive and endocrine disorders,” and also “diseases related to the respiratory and gastrointestinal system.”

(B) The nature of the invention claimed in claims 15 and 16 is that of a medical treatment method.

(C) At the time the present invention was made, in 2001 (applicants’ foreign filing date), cannabinoid CB1 receptor *antagonists* were known to be plausible as treatment for overeating and/or obesity. Compounds of the present invention are antagonists or inverse agonists at the CB1 receptor. Other utilities for antagonists of the CB1 receptor were hypothesized at the time the invention was made, but the only substantial utility for which evidence had been shown was reduction food intake. As evidence that reduction of food intake/treatment of obesity/treatment of overeating was a plausible utility for CB1 receptor antagonists at the time the invention was made, the examiner would cite:

Marzo et al, “Leptin-regulated endocannabinoids are involved in maintaining food intake” Nature, vol. 410, pages 822-825 (12 April 2001).

Agonists of CB1 receptor, on the other hand, were known to increase memory, decrease pain, and increase appetite among other things, at the time the invention was made. It appears that instant claim 19 embraces treatment of many disorders/diseases which are treatable with cannabinoid *agonists*, but not antagonists.

(D) The level of ordinary skill, with respect to the method claimed in claims 15 and 16 is that of a medical doctor, experienced in the treatment of the types of disorders and diseases recited in those two claims.

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(E) The level of predictability in the art of medicine is low; but it can be predicted that treatment of obesity, bulimia and extended abuse, addiction, and/or relapse indications could be achieved by administering a compound according to any one of claims 1 or 9-10 or by administering a formulation according to instant claim 12.

(F) Direction necessary for the practice of the method according to instant claims 15 and 16 is found in the instant specification at pages 17-19, wherein a recitation of basically the same scope of instant claims 15 and 16 is found. There is no delineation of dosages necessary for the treatment of the respective conditions recited in the claims, and no specific teachings relevant to practice of embodiments of claims 15 and 16.

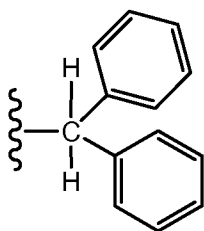
(G) There is no example of the treatment of any condition or disease, in a patient in need thereof, in the instant specification.

(H) Based on a consideration of the above factors, it is deemed that to grant applicants a right to exclude others from practicing a method commensurate in scope with claims 15 and 16 would be undue, in view of the amount of experimentation necessary for the realization of such a method.

Claim 1 is not enabled because one of the alternative definitions for R¹ and R² provides for a pentavalent carbon atom. The specification does not teach how to make the claimed formula (I) compounds wherein there is a pentavalent carbon atom is present in R³/R⁴. In the definition of R³/R⁴, the alternative -(CH₂)_r(phenyl)_s, wherein s is equal to 2, requires the CH₂- carbon atom immediately adjacent to the two phenyl rings to be pentavalent (having five bonds). As applicants are aware, the element carbon is normally

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capable of forming only four bonds with other atoms. When the value of “s” is 2, the substituent R³/R⁴ would have a structure including the group shown thusly:



the methylenic carbon atom would bear a formal negative charge, and although this negative charge could be stabilized by the aromatic ring systems, the compound having this functional group would undoubtedly be extremely difficult to isolate. These difficulties are not even alluded to in the disclosure. In fact the specification only teaches synthesis of diarylpyrazine compounds.

There have in fact been reports in the literature of synthesis of species where a carbon atom which is a ring member in a phenyl group atom has five bonding valencies, so compounds according to formula (I) wherein “s” is equal to 2 are theoretically possible, and as such are not automatically excluded from the scope of the instant claims as “inoperative embodiments” (inoperative embodiments are discussed in MPEP 2164.08(b)). As evidence of the fact that pentavalent carbon atom-containing compounds are possible to synthesize, the examiner would cite:

Martin, J.C. “‘Frozen’ Transition States: Pentavalent Carbon *et al*” *Science*, vol. 221(4610), pages 509-514 (5 August 1983).

Compounds “28” and “29,” appearing on page 513 of the article are compounds wherein a phenyl ring member is pentavalent, as would be the case in the instantly claimed formula (I) compounds wherein “s” is equal to 2. The instant specification does not provide any

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teaching sufficient to enable the skilled chemist to produce compounds of formula (I) analogous to the “frozen transition state” compounds comprising hypervalent carbon atoms which are described by Martin. An indefiniteness rejection under the second paragraph of this statute appears in the following pages, based on the grounds that it is not clear if applicants indeed intended to specify pentavalent carbon atom-containing species, or if some other bonding arrangement was intended for the situation where “s” is equal to 2. The factors from *In re Wands* have not been addressed in this finding of lack of enablement because it is believed that the deficiency prompting the rejection arose from an error in claim drafting. The rejection is actually necessary because the instant specification does not teach how to make certain of the claimed embodiments. The Wands factors will be addressed in a subsequent Office action if necessary, and more evidence presented.

Claims 1-9, 12 and 15-17 are indefinite under the second paragraph of 35 U.S.C. 112 because in the definition of R^3 and R^4 , one of the alternatives is a group – $(CH_2)_r(phenyl)_s$, wherein “s” is defined as “...1 when r is 0 otherwise s is 1 or 2...” It is not possible for there to be two phenyl rings bonded to a $-CH_2-$ group because there is available only one bonding valency on such a group. The $-(CH_2)-$ carbon atom would have to be pentavalent for there to be two phenyl rings (or any other type of substituent, for that matter) bonded thereto. Claim 1 is rendered indefinite by virtue of this deficiency because it is not clear whether or not applicants intended for there to be two hydrogen atoms on the is a group $-(CH_2)-$ carbon atom, or if applicants mistakenly defined “s” as being optionally 1 or 2, instead of only 1, or if applicants intended for there to be some intervening atom or linking group between $-(CH_2)-$ and phenyl (when r is a non-zero value), which would permit

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there to be two phenyl rings bonded at that position. In any case, claim 1 has been examined as though “s” were only equal to one, because that is the only permissible bonding arrangement.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 12, and 15-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 8, and 10-12 of copending Application No. 10/560,862. Although the conflicting claims are not identical, they are not patentably distinct from each other because at least two compounds named in claim 12 of the copending application are embraced by instant claims 1-4, and therefore also are embraced by instant claims 12 and 15-17. The first two named compounds in copending Application No. 10/560,862 are embraced by instant claim 1 wherein R¹ and R² are phenyl, substituted by “Z” wherein “Z” is 4-chloro-; R³ is (CH₂)_nCOOR⁷ wherein n=0

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and R⁷ is a C₄alkyl group; R⁴ is CONR¹¹R¹² wherein R¹¹ and R¹² are joined together with the nitrogen atom to which they are attached to form a saturated 6-membered heterocyclic group (piperidin-1-yl).

Since claim 6 of the copending application represents preferred species of claim 1 thereof, claims 1, 8 and 10-12 of the copending application have been included in this double patenting rejection.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Allowable Subject Matter

If the rejections set forth herein are overcome, the application will be allowed.

Claim 10 is allowed.

Conclusion

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Monday to Friday from 9:00am to 5:00pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

/Zachary C. Tucker/
Primary Examiner, Art Unit 1624